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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/822,698	03/30/2001	Hendricus R.J.M. Hoogenboom	DYX-015.1 US	5332

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EXAMINER

YAEN, CHRISTOPHER H

ART UNIT PAPER NUMBER

1643

DATE MAILED: 11/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/822,698

Applicant(s)

HOOGENBOOM ET AL.

Examiner

Christopher H. Yaen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 August 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-29 and 70-86 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 3 is/are allowed.
- 6) ☒ Claim(s) 1,2,4-29 and 70-86 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Re: Hogenbooboom et al

1. The amendment filed 8/26/2005 is acknowledged and entered into the record. Accordingly, claims 30-69 are canceled without prejudice or disclaimer, and claims 82-86 are newly added.
2. Claims 1-29 and 70-86 are pending and examined on the merits.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

4. It is noted that applicant amends the specification to remove the "http://" from the hyperlinked text. However, this does not overcome the instant objection because the hyperlink as currently amended is still an embedded hyperlink. Applicant is advised to spell out the term "www" to "world wide web".

Claim Rejections Maintained - 35 USC § 112, 1st paragraph

5. The rejection of claims 1-2, 4-29, 70-81 and now newly added claims 82-86 under 35 USC § 112, 1st paragraph as lacking an enabling disclosure is maintained for the reasons of record. Applicant argues that the instant claims as amended is supported by an enabling disclosure. Specifically, applicant indicates that the amendments to the claims to recite a MUC-1 specific binding member comprising a light chain and heavy chain variable region or portions thereof overcomes the rejection of record. Applicant

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also argues that the cited reference of Rudikoff *et al* does not provide any unpredictability in modifying the CDR regions of an antibody. Applicant states that "it is clear that Rudikoff does not teach that minor changes in variable regions of antibodies are likely to affect antigen binding function". Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record.

Although the amendments to the claims to recite both heavy and light chains variable regions have clarified some issues, the amendments to include a "portion" thereof still reads on a single CDR region. As indicated in the last office action, one of skill in the art would not be capable of using a single CDR region and yet maintain the same function activity of being specific for MUC-1 as claimed. Such a claim goes against the basic tenets of antibody binding theory as evidenced by Paul (Fundamental Immunology, 3rd Edition, 1993, pp. 292-295), wherein it is taught that of all antibodies requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs or hypervariable regions, which provide the majority of the contact residues for the binding of the antibody to its target epitope (see under "Fv Structure and Diversity in Three Dimensions"). In addition, Paul teaches that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. The instant specification has not provided one of skill in the art with any guidance regarding the use of a single CDR or the use of two CDRs in

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any conformation or orientation while maintaining specificity for the MUC-1 antigen.

Moreover, the conclusions made by the applicant regarding the interpretation of Rudikoff *et al* are merely arguments of counsel, which cannot take the place of factually supported objective evidence.

Applicant further argues that the instant specification provides one of skill in the art with guidance in the modification of amino acid substitutions through a process of affinity maturation and through the process of identify several amino acids which improve antibody affinity. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record. Specifically, the modifications taught in the specification only apply to a single CDR and the application has not taught the effects of such modifications in the context of a whole antibody or antigen binding fragment thereof.

Claims 18-27 are newly rejected under 35 USC 112, 1st paragraph because the claims are not enabled for a MUC-1 specific antibody or antigen binding fragment comprising an amino acid sequence that is 70-99% homologous to a single CDR. One of skill in the art would not be capable of practicing the invention because the artisan would not know how to use an antibody comprising a single defined CDR region that is 70%-99% homologous as claimed. The binding specificity as indicated above is made up of, at a minimum, 6 CDR regions (i.e. 3 from the heavy chain and three from the light chain) in a specific orientation in order for MUC-1 specific binding activity is to be maintained. Applicant has only provided a single source of CDR (i.e. SEQ ID No: 3 or CDR3) from the MUC-1 antibody. Without the rest of sequence information regarding

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the MUC-1 antibody, one of skill in the art cannot practice the invention. Moreover, the newly added claims (i.e. 82-86) or those claims that recite two or more CDR regions cannot be practiced without undue experimentation given the general nature and guidance of antibody binding (see Paul, cited above). Thus one of skill in the art would neither expect nor predict the appropriate functioning of the antibody as broadly as is claimed.

All other rejections are withdrawn in view of the applicant's amendments and arguments thereto as set forth in a paper filed on 8/26/05.

Conclusion

Claim 3 appears to be free of the prior art. Claims 1-2, 4-29, and 70-86 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H. Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen
Art Unit 1643
November 10, 2005



CHRISTOPHER YAEN
PATENT EXAMINER